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(Amersham Pharmacia Biotech, Piscataway, NJ), such as crosslinked or non-crosslinked, agarose, SEPHAROSE, dextran, silica containing polymer, organic polymers (natural or synthetic), a ceramic-containing, or a gel matrix, backbone, or a combination of any of these, with C₃ to C₁₀ alkyl, branched or straight, pendent side chain ligands. Preferred pendent ligands include propyl, butyl, hexyl and/or octyl ligands. These ligands provide the preferential binding interaction which is exploited in the separation, purification and/or isolation methods of the present invention. One of ordinary skill in the art will appreciate that hydrophobic interaction resins may include ligands in addition to or in place of these alkyl ligands, which will also be useful in the method of the present invention. Examples of such ligands include, but are not limited to, phenyl, octyl, butyl, propyl, neopentyl, hydroxypropyl, benzyl, octadecyl, diphenyl, and methyl as well as substituted and unsubstituted derivatives of same, and combinations thereof. Suitable resin or media materials useful in the present invention include those described, for example, in EP Patent No. 964057, EP Application No. 99109441, JP 2000035423, JP 99127700 and JP 98127665 (Kitamura et al.) the entire contents of each of which are hereby incorporated by reference.--

Page 20, delete the paragraph spanning lines 9-14 and insert the following therefor:

Q2

-- The beads used in STREAMLINE (Chromatography column, including media available from Amersham Biosciences for expanded bed adsorption separation) columns typically are larger in size with different densities, and are made by various manufactures, including Amersham Pharmacia Biotech, Biosepra Inc, but not limited to

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these, where the clarified lysate could be flowed through these "expanded bed"
columns, resulting in removal of contaminants through binding to the beads that contain
the hydrophobic interactive ligands.--

Pages 21 to 22, delete the paragraph spanning page 21, line 21 through page
22, line 5 and insert the following therefor:

Q3
-- Figure 4 (insert) shows a scanned image of an agarose gel from Example 5
(butyl HIC) stained with SYBR GOLD (Stain available from Molecular Probes for
staining nucleic acids on agarose gels) wherein lane 1 contains a supercoiled DNA
Ladder; lanes 2 and 3, contain samples from peak 1 (relaxed) and lanes 3-5 contain
samples from peak 2 (supercoiled). (Lanes being numbered from left to right.) The
chromatogram from Example 5 of absorbance versus volume shows the separation of
relaxed (peak 1) and supercoiled DNA (peak 2).--

Page 28, delete the paragraph spanning lines 1-16 and insert the following
therefor:

Q4
--An attractive feature of this method of endotoxin removal is the immense
capacity of the resin for the endotoxin, of approximately 1,000,000 EU/ml of resin, in
addition to the simplicity and >95% recovery of plasmid DNA. For example, a plasmid
DNA solution containing 500 mg of plasmid and 10 million EU of endotoxin can be
purified using 10 ml of resin, whereas, at least 1,000 to 4,000 ml of an anion exchange
resin would be required for binding the plasmid DNA and the endotoxin, with the added
disadvantage of poor recoveries on such an anion exchange resin. The method of the
present invention therefore results in savings of 100 to 400 fold in resin cost, and

additional savings on column cost and increased recovery of product. The commercially available DNA Etox resin is currently at least 8 fold more expensive than the resins used in the method of the present invention. Another commercial resin (POLY-FLO (Chromatography media available from PureSyn Inc. for plasmid DNA purification) – PureSyn Inc., 87 Great Valley Pkwy Malvern, PA 19355) with proprietary chemistry that is useful in endotoxin removal is 5 to 10 fold more expensive and requires the use of solvents and ion-pairing chemicals.--

Pages 32 to 33, delete the paragraph spanning page 32, 17 through page 33, line 13 and insert the following therefor:

--A Butyl 650S column (Butyl 650S resin from TosoHaas Inc., 156 Keystone Drive, Montgomeryville, PA 18936) of 2.6 cm diameter and 15 cm bed height, of approximately 75 ml bed volume was packed and equilibrated with TE buffer, pH 7.4, containing 2M AS. The sample was loaded at a flow rate of 5 ml/min. The flow through was collected, and samples were taken for analysis (DNA concentration, agarose gel, and endotoxin assay. Endotoxin assay was performed with spikes and samples were diluted appropriately to obtain PPC (Positive Product Control) recoveries in the range considered acceptable. Endotoxin concentrations were determined using the BioWhittaker KINETIC-QCL (Endotoxin assay kit available from BioWhittaker) Chromogenic LAL assay as described in BW publication No. P50-650U-5, KINETIC-QCL Test Kit Manual. Following the sample load, TE containing 2M ammonium sulfate was flowed through the column, and collected and sampled. The column was subsequently washed with TE buffer - pH 7.4, USP purified water, and cleaned with

0.5N sodium hydroxide, and rinsed with >15 volumes of USP purified water. Endotoxin was present in each of these washes as shown below in Table 1. In addition to this outstanding endotoxin removal efficiency, significant amount of RNA, protein, and DNA fragments were removed, leaving the sample significantly purified.--

Page 46, delete the paragraph spanning lines 1-15 and insert the following therefor:

-- *E. coli* cells harboring the plasmid pE1A-K2 was grown, and lysed using chemical methods, and clarified through centrifugation methods. The supernatant was used for the experiment. The sample was purified through an anion exchange column (Q-HYPER D (Anion exchange chromatography media) – BIOSEPRA Inc.). A 2M sodium chloride elution from the column was used for this experiment. The sample was present in 50mM Tris 10mM EDTA pH 7.4 buffer with 2M NaCl. A Butyl HIC column (using Butyl 650S resin – TosoHaas) of diameter 1 cm and height 20 cm of approximately 10ml volume was packed and equilibrated with TE containing 2M sodium chloride. The sample was loaded at a flow rate of 2 ml/min. The flow through was collected, and samples were taken for analysis (DNA concentration, agarose gel, and endotoxin assay). Following the sample load, TE containing 2M ammonium sulfate was flowed through the column, collected and sampled. The column was subsequently washed with TE pH 7.4.--